Guidance

FDA's "Drug Watch" for Emerging Drug Safety Information

DRAFT GUIDANCE

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For questions regarding this draft document contact Deborah Henderson, (301) 594-5400.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

May 2005
Drug Safety

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Office of Training and Communications
Division of Communications Management
Drug Information Branch, HFD-210
5600 Fishers Lane
Rockville, MD 20857
(Tel) 301-827-4573
(Internet) http://www.fda.gov/cder/guidance/index.htm

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This guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

I. INTRODUCTION

This document provides guidance on how FDA intends to develop and disseminate important emerging drug safety information concerning marketed drug products[2] to healthcare professionals and patients. This information will appear on an FDA Web page to be called the "Drug Watch."[3]

The Drug Watch is intended to identify drugs for which FDA is actively evaluating early safety signals. The Drug Watch is not intended to be a list of drugs that are particularly risky or dangerous for use; listing of a drug on the Drug Watch should not be construed as a statement by FDA that the drug is dangerous or that it is inappropriate for use. Rather, inclusion on the Drug Watch signifies that FDA is attempting to assess the meaning and potential consequences of emerging safety information.

All drugs have risks, and prescribers must balance the risks and benefits of a drug when making judgments about an individual patient's therapy. Sometimes after a drug is approved, rare but serious side effects emerge as the drug is more widely used or is prescribed for off-label uses. Sometimes emerging risks appear to be life-threatening, while in other cases they may appear to be less serious. In most instances, however, there is a period of uncertainty while FDA and the drug's sponsor evaluate new, emerging safety information to determine whether there is a real safety concern related to the drug and whether regulatory or other action is appropriate. The purpose of the Drug Watch Web page is to provide a forum in which we can communicate emerging safety information to the public while we continue to evaluate that information. We intend to work as quickly as possible to assess and address the potential safety issues identified on the Drug Watch.

[1] This guidance has been prepared by the Office of Regulatory Policy in the Center for Drug Evaluation and Research (CDER) at the Food ad Drug Administration (FDA).

[2] The phrase *drug products* as used in this guidance includes all drug and biological products regulated by CDER. Marketed drugs included on the Drug Watch may be approved or unapproved drugs, used for approved or unapproved uses.

[3] The Drug Watch page will be available at FDA's WEB site, www.fda.gov.

Moreover, we will continue to communicate important information about drug risks that are known with greater certainty using traditional means, such as public health advisories.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited.

II. BACKGROUND

FDA has long provided information on drug risks and benefits to healthcare professionals and patients when that information has generated a specific concern or prompted a regulatory action, such as a labeling change. Because of recent questions related to drug safety, however, FDA is reexamining its risk communication program, including how and when we communicate emerging risk information to healthcare professionals and patients.

Increasingly, patients are taking a more active role in their healthcare. Patients want information about the products they are taking, and patients actively seek the information they want from different sources, including, for example, the Internet. Patients and their healthcare providers rely on the information from these sources to make important prescribing and treatment decisions. FDA has concluded it should do more to make drug risk information available as it emerges while the Agency is evaluating its significance. We want to make sure that patients and their healthcare providers have quick access to the most up-to-date and emerging product information available in an easily accessible form. As a result, we are taking steps, described below, to make important emerging drug safety information available to healthcare professionals and patients in a new format and earlier than we have in the past. Our goal with the Drug Watch is to share emerging safety information before we have fully determined its significance or taken final regulatory action so that patients and healthcare professionals will have the most current information concerning the potential risks and benefits of a marketed drug product upon which to make individual treatment choices.

III. DISCUSSION

A. What information will be posted?

We have decided to develop a page on our Web site, known as the "Drug Watch," that will provide information about drugs with significant emerging safety issues that FDA is evaluating. The factors FDA intends to consider in determining whether to post such information about a drug on the Drug Watch are described in section III.B., below.

For some drugs, the Web page will contain factual information about newly observed, serious adverse events associated with the use of a drug that have been reported to FDA.

For example FDA might post the following for Drug A:

> FDA is investigating postmarketing reports of renal failure in elderly patients treated with Drug A, but a causal relationship has not been established. We are continuing to analyze these reports to determine whether the occurrence of these adverse events affects the risk/benefit assessment of Drug A therapy.

Although sponsors are likely to be aware of these emerging potential safety issues, often patients and healthcare professionals do not become aware of the emerging information until we or the sponsors take some action.[4] Posting this information on the Web site will alert patients and healthcare professionals to potential safety risks while FDA is still evaluating the strength of the relationship between the drug and the adverse event.

For other drugs, the Web page may contain information about significant emerging risks that FDA believes may be associated with a drug, but that might be avoided by appropriate patient selection, monitoring, or use of concomitant therapy. This type of information is illustrated by the following:

> Drug B has been associated with serious skin reactions in patients allergic to eggs. Prescribers should consider this information when treating patients with these allergies.

A third category of information might be posted on the Drug Watch when an important risk minimization procedure is put into place by a sponsor in response to emerging information. Announcing the new procedure on the Drug Watch will alert patients and healthcare professionals to important changes in how a drug should be prescribed, dispensed, or used. For example:

> The sponsor for Drug C has determined that Drug C can cause liver damage in patients with impaired liver function. The sponsor has advised prescribers to check a patient's liver enzymes before the drug is prescribed and at regular intervals thereafter.

Most of the information that will be posted on our Web site is information that is now made available to the public (after proper redaction of confidential commercial and personal privacy information) in response to Freedom of Information Act (FOIA) requests. Because of the importance of this information to healthcare professionals and patients, we have decided to take steps to make such emerging information available without waiting for a FOIA request, even before we have reached conclusions about that information that might prompt a regulatory action (such as relabeling the drug).

For emerging safety information that we are still evaluating, we will accompany the information with a disclaimer such as the following: "This information reflects FDA's preliminary analysis of data concerning this drug. FDA is considering, but has not reached a final conclusion about, this information. FDA intends to update this web page when additional information or analyses become available."

[4] Sponsors are the most frequent source of reported information about serious side effects, and FDA regularly discusses emerging risk information with sponsors to further its evaluation of the information and determine an appropriate course of action. The purpose of the Drug Watch is to disseminate this information to the public while FDA evaluates it so that patients and practitioners may consider the information as well.

As part of implementing the Drug Watch, we also intend to provide information about the status of our analysis of an emerging safety issue. We might say, for example, that we have not yet determined whether the reported side effects have been caused by the drug, but we are continuing to analyze the data. In other instances, we might say that we have concerns and intend to take the issue to a public advisory committee. We intend to update the information on the Drug Watch frequently as new information becomes available or specific issues are resolved.[5]

As noted, the purpose of the Drug Watch Web page is to communicate significant emerging safety information about specific drug products or classes of drug products. This emerging safety information may relate to new risks, new information on known risks, or risks associated with off-label uses. By definition, however, the information posted on the Drug Watch is information about which FDA has made no final regulatory judgment. Posting information on the Drug Watch Web page does not mean that FDA has concluded there is a causal relationship between the drug product and the risks or adverse events described. Such posting also does not mean FDA is advising practitioners to discontinue prescribing the products that appear on the Drug Watch. Instead, our goal is to make emerging safety information available to the public so that healthcare professionals and patients can consider the information when making decisions about a patient's medical treatment.

Information will be posted with or without redactions in accordance with applicable disclosure laws and FDA regulations.

B. How will FDA decide which drugs will be included on the Drug Watch?

FDA has identified several factors that it plans to consider when deciding which drug products and information to include on the Drug Watch:

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[5] We also have decided to intensify our current program to provide the public with the most important information for the safe and effective use of drugs in patient friendly language. As part of this continuing effort, we are developing *Patient Information Sheets* intended to convey critical facets of a product's approved labeling in lay terms. These sheets will include a section for "emerging safety information" in those instances when we determine that there is information on the Drug Watch that a patient should consider. This "emerging safety information" will match the information on the Drug Watch. Information from the Drug Watch that is not in the final labeling of the product will be clearly delineated and segregated along with the following disclaimer: "This information reflects FDA's preliminary analysis of data concerning this drug. FDA is considering, but has not reached a final conclusion about, this information. FDA intends to update this sheet when additional information or analyses become available." Our ultimate objective is to develop Patient Information Sheets for all approved drugs, most of which will not have an emerging safety section.

We are also continuing to develop *Healthcare Professional Information Sheets*, which we ultimately intend to develop for all new molecular entities as well as some other drugs. These sheets are intended to highlight the most up-to-date information healthcare professionals may want to consider when prescribing drugs for their patients. This is not a new approach. When available, the highlights section of a product's approved labeling will be used to develop the Healthcare Professional Information sheets. We have already posted some patient and healthcare professional information sheets on our Web site for drugs with recent emerging safety issues. See for example, Celebrex patient and professional sheets, http://www.fda.gov/cder/drug/infopage/celebrex/Celebrex-ptsk.pdf and http://www.fda.gov/cder/drug/infopage/celebrex/celebrex-hcp.pdf. We intend to link the information that is on Drug Watch to patient and healthcare professional information sheets when they are available.

- Whether new and emerging safety information could significantly affect prescribing decisions or how patients should be monitored (e.g., a drug that has been identified with a possible association with renal failure should not be prescribed to patients with renal disease; a new possible drug-drug interaction has been identified and needs to be considered in prescribing)
- Whether measures can be taken as a result of providing information that could help to prevent or mitigate harm (e.g., limit prescribing to patients most likely to benefit from the drug, conduct special monitoring of patients on the drug, be alert for signs of serious adverse reactions)
- Whether an unapproved (off-label) use of the drug appears to pose a significant risk to patients

We may also consider other factors as appropriate.

Before posting information on the Drug Watch, we plan to conduct at least a preliminary analysis to determine that the new safety information is sufficiently credible to warrant public dissemination. We intend to post emerging information about a drug on the Drug Watch only when we believe that the data are significant enough to warrant further consideration to determine whether an actual safety problem exists.

We have established a Drug Safety Oversight Board that will be responsible for managing important emerging drug safety issues in the CDER and the Drug Watch program. This Board will decide which products (or classes of products) to include on the Drug Watch using the preceding factors, and, using the factors described below, will determine when drugs are removed from the Drug Watch. The Board will also manage the process for determining what information will appear on the site with regard to particular drugs.

The Board will include representation from the following CDER Offices:

- Office of Drug Safety
- Office of New Drugs
- Office of Counter Terrorism and Pediatric Drug Development
- Office of Medical Policy
- Office of Compliance
- Office of Pharmaceutical Sciences
- Office of Clinical Pharmacology and Biopharmaceutics
- Office of Biostatistics

In addition, the Board will have a permanent member from outside of CDER from each of the following:

- FDA's Center for Biologics Evaluation and Research
- FDA's Center for Devices and Radiological Health,

- A non-FDA Department of Health and Human Services (DHHS) agency (e.g., the National Institutes of Health)
- A non-DHHS healthcare providing agency (e.g., the Veterans Administration or the Department of Defense).

The Board also may engage as consultants the Chairs of FDA Advisory Committees and other external scientific experts, as well as consumer and patient representatives to present their views regarding emerging drug safety issues.

C. How will drugs be removed from the Drug Watch?

FDA plans to regularly update the information on the Drug Watch Web page as new information becomes available. As safety issues are resolved, FDA intends to promptly remove drugs from the Drug Watch. For example, a drug may be removed from the Drug Watch when its labeling has been revised to address the safety concerns, when FDA has taken other steps to adequately communicate information to healthcare professionals and patients, or when FDA has determined that, despite the initial signals, there is no new safety concern.

D. Will sponsors be notified that a drug will be placed on the Drug Watch?

FDA intends to notify the relevant sponsor that information about its drug will be placed on the Drug Watch shortly before the first instance in which information about that drug is posted on the web site.

E. How will the Drug Watch affect the promotion of prescription drugs?

FDA recognizes that some sponsors may consider drawing promotional comparisons between their products and products that appear on the Drug Watch (e.g., by suggesting that the appearance of a drug on the Drug Watch necessarily signals a serious problem and/or by using the information posted on the Drug Watch as the basis for a comparative claim). In turn, some sponsors whose products appear on the Drug Watch may want to minimize the effects of the information that FDA has made public.

We remind sponsors that all safety and effectiveness claims made in prescription drug promotion, including claims based on government materials such as the Drug Watch, must be supported by substantial evidence or substantial clinical experience, and must not be otherwise false or misleading (21 U.S.C. 355 and 352; 21 CFR 202.1(e)).

Neither the fact that a drug appears on the Drug Watch nor the specific information posted about that drug will generally constitute (either separately or collectively) substantial evidence or substantial clinical experience to support a comparative safety or effectiveness claim. Therefore, comparative claims made in prescription drug promotion based on information on the Drug Watch (e.g., "Our drug is safer because of the adverse event information posted on the Drug Watch about a competitor's drug"; or, "Our drug is safer because it is not on the Drug Watch") may be considered false or misleading.

Representations made to minimize the effect of emerging risk information on the site may also be considered false or misleading. For those seeking to explain to healthcare professionals what, if anything, it means to appear on the Drug Watch, we refer you to the sections of this guidance that discuss the purpose of the Drug Watch Web page and the nature of the information to be posted on the site.